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GRANT NUMBER DAMD17-97-1-7279

TITLE: Correlative Study of Tumor Hypoxia and Metastatic Potential in Breast Cancer

PRINCIPAL INVESTIGATOR: Mahesh A. Varia, M.D.

CONTRACTING ORGANIZATION: University of North Carolina

at Chapel Hill

Chapel Hill, North Carolina 27599-1350

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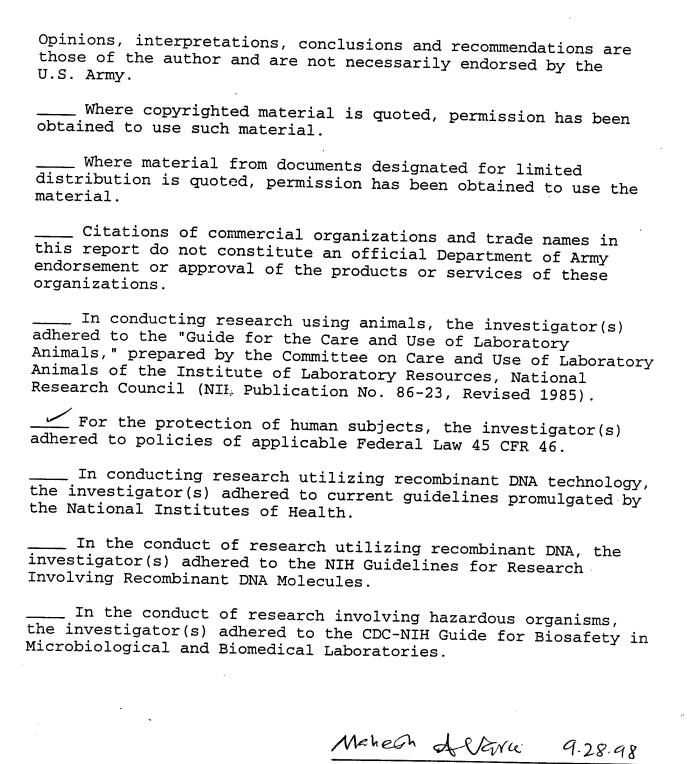
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immunohistochemical binding, of hypoxia with markers of cel Scope: The specific aims are: I: Determine the presence and to hypoxic tumor cells. II: Determine the patterns of blood vessels and necrosis. III: Correlate the presence ar metastases. IV: Correlate the presence an PCNA, Ki-67, and VEGF. V: Monitor adverse effects of Major Findings: The clinical	ells. Does the presence of correlate with the presence of proliferation, p53, apoptosis, a extent of tumor hypoxia in bio pimonidazole binding in the broad extent of tumor hypoxia in pd extent of tumor hypoxia with	hypoxia in breast primary axillary lymph node metastase and VEGF in the primary breast cancer passes of primary breast cancer east cancer biopsies in relation primary breast cancer with the the presence of other biological. Please see the Annual Report	detected by pimonidazole s, and correlate the presence st tumor tissue. using pimonidazole binding a to other landmarks such as the presence of axillary node call markers: p53, apoptosis, ort Statement. 8 or earlier pending Review
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FOREWORD



PI - Signature

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Annual Report Statement



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September 28, 1998

For Attention of MCMR-RMI-S Research Data Management

SUBJECT: Annual Report for Grant DAMD17-97-1-7279

Ms. Judy Pawlus

Office of the Deputy Chief of Staff for Information Management

U.S. Army Medical Research and Materiel Command

504 Scott Street,

Fort Detrick, MD 21702-5012

Dear Ms. Pawlus,

Enclosed please find the following in reference to the Annual Report for Grant DAMD17-97-1-7279.

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- **Annual Report Statement**

Please note that this research project has been delayed on account of issues related to the Consent for Human Subjects as described in the Annual Report Statement and we are hoping to commence patient entry this fall for research on this grant.

Request for Deferral of Protocol Start Date: We request a deferral of the start date of the clinical research protocol to November 1st, 1998 or earlier pending Reveiew Committee approval.. This should complete all the required approvals of the involved Human Research Review Boards and adherence to policies of applicable Federal Law 45 CFR 46. Explanation for this request is provided in the attached Annual Report Statement.

Sincerely,

Mahesh A. Varie

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Professor,

Department of Radiation Oncology

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Enc.

Annual Report Statement Grant DAMD17-97-1-7279

There has been a lag in obtaining the approval of the Informed Consent Form for participation by breast cancer patients on the research study funded by this grant. After the initial award of the grant, a number of changes in the Consent Form approved by our Institutional Review Board were requested by the Surgeon General's Human Subjects Research Review Board (HSRRB, HURRAD Log. No. A-7766), USAMRMC Human Subjects Protection Division.

Although most of these changes could be addressed without significant difficulty, a major problem related to provision of financial compensation for research subjects in the event of research related **injury**. The required language of the two Review Boards were in direct conflict. In the Consent Form, our Review Board requires that in such a situation, provision will be made for medical care to the research subject but the institution cannot assume financial responsibility. HSSRB required that provision be made of financial responsibility. According to the Senior Legal Counsel of the University of North Carolina, the State of North Carolina does not permit the University to assume such responsibility.

After further discussions on this subject, language acceptable to both Review Boards was developed whereby Department of Defense as the sponsor of the research assumes the financial responsibility. These deliberations and required approval of the Consent Form has delayed entry of research subjects entry into the research protocol for this grant.

Pending final clarifications to the Clinical Research Advisory Committee our General Clinical Research Center (GCRC) regarding the cost of the research component of the tumor biopsy procedure, full approval of the clinical protocol is anticipated at the Committee's next meeting next month. The GCRC has indicated its enthusiastic approval of the protocol and unanimous support of the research proposal.

In view of the above deliberations and in order to comply with the requirements of the Human Research Review Boards of the DOD, University of North Carolina, and the GCRC, we have not embarked on the enrollment of patients.

Request for Deferral: We request a deferral of the start date of the clinical research protocol to November 1st, 1998 or earlier as expected with the GCRC approval. This should complete all the required approvals of the involved Human Research Review Boards and adherence to policies of applicable Federal Law 45 CFR 46.

We are extremely excited and enthusiastic about this innovative research and are very anxious to proceed with patient enrollment in compliance with the applicable approvals.

Revised, 9/30/98.